Vol. 4 No. 3. March, 1945

ANNALS OF THE RHEUMATIC DISEASES

CONTENTS

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (4 NUMBERS) 25/- U.S.A. $6.00 SINGLE NUMBER 7/6

NOTICE TO SUBSCRIBERS

Subscriptions are payable to the British Medical Association. Address: British Medical Association House, Tavistock Square, London, W.C.1.

NOTICE TO CONTRIBUTORS

Papers submitted to this Journal are accepted on the understanding that they have not been and will not be published in any other journal, and are subject to editorial revision. All papers and other editorial communications should be addressed to Dr. C. W. Buckley, 5, The Square, Buxton, Derbyshire.

The author of an original article should make adequate references to previous work on his chosen subject.

A full summary of his observations and conclusions must be given.

A paper describing a single case will not be accepted unless the case is sufficiently rare, or shows important features not previously described, or has been made a subject of special observation or experiment.

Articles must be as concise as possible and be typewritten on one side of the paper only, with double spacing and a margin of not less than 1¼ inches. Only recognized abbreviations should be used. Graphs, charts, tables, and legends for them should be presented on separate sheets and not included in the text. When half-tone reproduction of x-ray illustrations is required, the author is advised to send the original film unless he wishes to bring out special points in a print of his own choice. Photographs and photomicrographs should be printed on glossy paper, should be larger than the size desired for reproduction, and, if transmitted through the post in a tube, should be rolled with the picture outside. With the exception of letters and numbers, which should be lightly written in pencil, everything that is to appear in the reproduction of a graph or chart should be carefully drawn in black ink on tracing linen, or Bristol board, or stout, smooth, white paper.

References should be arranged according to the Harvard system. In the text, the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (*a*, *b*, *c*) after the date. No numbering of references is necessary. At the end of the contribution references are arranged in the alphabetical order of the author's names. The reference details are given as follows: Author's name and initials, year of publication (in parentheses), title of periodical (in italics, abbreviated according to the *World List of Scientific Periodicals*), volume number (bold type, Arabic numerals), and first page number (ordinary type, Arabic numerals), thus:

Cowan, J. (1929). *Quart. J. Med.*, **22**, 237.

When a book is referred to, the full title, publisher, the place and year of publication, edition and page number should be given.

Contributors will receive one proof in page, but it is assumed that all but verbal corrections have been made in the original manuscript; an allowance at the rate of ten shillings per sheet of sixteen pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Fifty free reprints of articles will, if desired, be given to contributors. A limited number of additional reprints at cost price can be supplied if application is made when returning proofs. An estimate of costs will be given on application to the Publishing Manager, British Medical Association.

Papers which have been published become the property of this Journal, and permission to republish must be obtained from the Editors.

Application for Advertisement space should be addressed to the Advertisement Manager, British Medical Association, Tavistock Square, London, W.C.1.

fr
ab
ex
so
en
fr
th
ur
ar
ty
a
ar
te
ca

se
ca
ar
hy
by
M
19
o
b
th

in
o
5
d
n
p
c
o
la
a
o
h
t
c
t
o
s
i
p
s

GOUT AND ITS EFFECT ON THE CARDIOVASCULAR SYSTEM *

BY

G. LEROY STEINBERG

The characteristic feature that distinguishes gout from the other syndromes of rheumatic disease is an abnormality of uric acid metabolism. Uric acid exists in the body both as free acid and as the more soluble monosodium salt. Approximately half is endogenous in origin and the remainder is derived from digestion of nucleoproteins and nucleic acid in the food. The total amount of urate excreted in the urine is normally about 0·75–1·00 gramme per day, and the quantity is increased by ingestion of any type of protein and decreased by a high fat diet—a mechanism utilized by Lockie and Hubbard (1935) and Lockie (1942) in order to test for gout by attempting to promote an acute attack in a suspected case by placing him on a ketogenic diet.

Since the time of Thomas Sydenham (1683), himself a sufferer, gout has been blamed as one of the causes, or at least a concomitant, of kidney damage and renal calculus. The frequent occurrence of hypertension and vascular lesions in gout is recorded by many authorities (Meakin 1939, Osler and McCrae 1925, Cecil 1943, Levine 1940 and Stotzer 1939), while Garcin (1939) gives a detailed description of the histology of the gouty kidney. Only Rosenbloom (1918) and Buckley (1937, 1938) state that this association is not constant, and often absent.

Master and others (1943) have estimated that the incidence of hypertension in persons over 40 years of age in the general population is not more than 50 per cent. The term hypertension in their report denotes (1) a systolic pressure of 150 mm. Hg or more at any time during observation, (2) a diastolic pressure of 96 mm. or more prior to an attack of coronary occlusion, (3) a diastolic pressure of 90 mm. or more during or after the attack, (4) marked enlargement of the heart without obvious cause. The application of these criteria shows that 69 per cent. of the patients afflicted with coronary occlusion had hypertension before the attack. The incidence in the general population, including men, women, and children, is much less than Master's figures. During the past ten years, 83,514 patients were admitted to one of our large local general hospitals. During a similar period 10,073 patients with either coronary insufficiency or coronary occlusion, and 1,819 patients with essential hypertension (with no demonstrable coronary disease), were admitted.

* This is an abridgment of an article submitted for publication.

Present Investigation

Forty-six cases of typical gout are included in this study. All the patients have been observed and treated by the writer, and most of them have been observed over a period of several years. The age of a patient listed in Table 1 is the age at which the patient was first seen. Thirty-one patients had a normal blood pressure (Table 2) and 15 had hypertension (Table 3). Only 2 patients of the hypertensive group were under 45 years of age. If one assumes that the average percentage of hypertension occurring in adults past the age of 45 is 50, then hypertension among the gouty is no higher than in the average population. However, a more convincing argument against the view that gout produces hypertension is a study of the duration of the disease and its effect on the blood pressure. Eighteen cases of gout in the non-hypertensive group had their gouty symptoms for a period of five years or over; 13 cases had clinical gout for a period of ten years or over, 9 cases for a period of fifteen or more years, and 4 for a period of at least twenty years. Most impressive is the fact that Case 13, that of a white male aged 72, had a history of recurrent attacks of gout for a period of forty years and still had a normal blood pressure. No cardiac enlargement and no symptoms of angina were present in the non-hypertensive group. Two patients developed hypertension while being observed. The blood pressure in one case rose from 140/100 to 190/110 during a period of four years, and the blood pressure in the other case rose from 140/80 to 160/106 during a period of two years' observation. The first case had gout for a period of nine years, and the second for twenty years.

Nine cases of gout revealed a trace to a 1+albumin in the urine at different periods of observation. Three of these nine cases also had hypertension. The ages of these patients varied from 45 to 62 years. Only one patient of the entire group of 46 cases had a renal calculus, which was present seven years before the onset of the clinical gout. The ability of the kidney to concentrate was good in all 46 cases, as demonstrated by a urine with a specific gravity of 1020 or higher.

Symptoms of angina were present in three cases. Two of these patients had hypertension. One patient aged 39 years had had gout for five years,

TABLE I

A CLINICAL INTERPRETATION OF GOUT

Case	Sex	Age	Duration	Blood pressure	Heart	E.C.G.	Weight	Urine
1	M	57	10 years	140/80	Negative.		150/140	Negative.
2	M	60	5 ,,	124/90	,,		155/154	,,
3	M	51	24 ,,	160/80	Systolic and diastolic, base and apex.		177/184	Trace albumin; occasional hyalin cast.
4	M	47	7 months	140/110	Negative		224/198	Negative.
5	M	39	3 years	140/100	,,		170/144	,,
6	M	53	7 ,,	120/80	,,			,,
7	M	68	20 ,,	120/80	,,			Faint trace albumin
8	M	56	10 ,,	114/80	,,			Negative.
9	M	42	4 ,,	120/80	,,		202/194	,,
10	M	51	5 ,,	120/80	Systolic, apex and base.		188/157	,,
11	M	61	10 ,,	180/100	Systolic, praecordium.		178/142	,,
12	M	41	7 ,,	136/90	Negative.		207/174	Albumin, +. Occasional granular cast.
13	M	45	2 ,,	140/80	,,		175/151	Negative.
14	F	53	6 weeks	170/100 (Cerebral haemorrhage 4 years later.)	,,	Negative.	165/148	,,
15	M	39	13 years	120/72	,,	,,	250	Rare hyaline cast.
16	M	40	14 ,,	120/80	,,			Negative.
17	M	45	4 ,,	120/80	,,	,,	175/153	,,
18	M	55	4 months	120/80	,,		165/149	Trace albumin.
19	M	47	9 years	140/90 and four years later 190/110.		,,	183/163	Albumin, +.
20	M	39	5 ,,	150/120	Angina.	,,	170	Negative.
21	M	53	2 ,,	124/80	Negative.		159/169	,,
22	M	46	7 ,,	120/80	Negative.	Slight notching P waves all leads.	150	,,
23	M	50	7 weeks	120/84	,,			,,
24	M	49	18 years	120/90	,,			Albumin, +.
25	M	66	10 ,,	190/94	Angina; left ventricle enlarged.		193/156	Negative.
26	M	45	16 ,,	140/90	Systolic (apex).		155/162	,,
27	M	47	5 months	130/90	Negative.		180/152	,,
28	M	56	27 years	120/70	Angina.		180/155	,,
29	M	58	3 ,,	126/78	Negative.	Q.R.S. slurring all leads.		,,
30	M	31	3 months	136/76	Soft systolic murmur, praecordium.	Slurring Q.R.S. all leads.		,,
31	M	50	20 years	140/80	Negative.		155/161	,,
32	M	59	1 year	140/80	Loud apical systolic murmur.		150/147	,,
33	M	48	1 month	150/80	Negative.			,,
34	M	62	27 years	130/78	,,	Slurring Q.R.S. all leads.		,,
35	M	48	9 months	104/60	,,			,,
36	M	48	17 years	135/90	,,	Notched P waves, and slurring Q.R.S. all leads.		Trace albumin.
37	M	62	4 ,,	160/86	Slight enlarged left ventricle.			Trace albumin; rare hyalin cast.
38	M	55	2 ,,	150/100	Negative.			Negative.
39	M	72	40 ,,	145/70	,,			,,
40	M	43	2 ,,	145/100 (112/70 four years before onset.)	,,			,,
41	M	69	2 months	180/100	Old infarct by E.C.G.			,,
42	M	49	2 years	120/80	Negative.			,,
43	M	49	18 ,,	120/90	,,		174/162	,,
44	M	49	3 weeks	150/86	,,		Overweight.	,,
45	M	57	1 week	140/80	,,	Slight slurring all leads.		
46	M	50	20 years	140/80 (2 years later 160/106	Enlarged left ventricle.	Slight slurring all leads.		,,

the second, aged 66, for ten years, and the third, aged 56, for twenty-seven years.

Drugs in the Treatment of Gout

There is little question that the prevention of acute attacks of arthritis is desirable. More is gained by this prophylaxis than the mere comfort of the patient, for chronic gouty arthritis with its destructive joint changes is thus prevented. The use of cinchophen, a hepato-toxic agent, would be profitably replaced by colchicine if found equally efficacious. The following safe and effective method has been employed with this end in view. The patient with an acute attack of gouty arthritis is placed on absolute bed rest. A low-fat, high-carbohydrate, restricted nucleo-protein diet is prescribed. All alcoholic beverages and all activities which place an unusual stress or strain upon the joint are prohibited. Colchicine—1/100 grain (0·65 mgm.)—is given by mouth every hour until one of two things occurs. Either the patient develops diarrhoea or the acute joint symptoms subside, usually after taking twelve to eighteen tablets.

The drug is then stopped for twenty-four hours and resumed later, on a reduced dosage of one tablet three times daily. The exact amount required to produce either the diarrhoea or the relief of joint symptoms is noted in the record, an observation of use if the patient subsequently appears to be developing an acute attack of arthritis, or if the blood uric acid rises to a level above 5 mg. per 100 c.cm. The patient should then be given colchicine just short of the dosage that formerly produced gastro-intestinal symptoms. Blood uric acid estimations are necessary at three to four weekly intervals in order to carry out this control. If the blood uric acid is under 5 mg. per 100 c.cm. and no joint symptoms are present, it is reasonably safe to continue one tablet of colchicine three times daily until the next examination.

Many patients who were nearing the so-called gouty arthritic stage, in which they were getting attacks as frequently as every six weeks, have remained symptom free and in constant employment under this management. Colchicine is a much safer drug than cinchophen. No unusual findings in the electrocardiograph, and no change in the blood pressure or the pulse were observed in a patient who had received as many as twenty-two 1/100-grain tablets of colchicine at hourly intervals. Occasionally, however, one finds a gouty patient who does better with large doses of salicylates than with colchicine. These people may be placed on 60 to 80 grains of salicylates for three days of the week and colchicine 1/100 grain three times daily for the remainder of the week. This regimen is also useful for those who develop gastro-intestinal symptoms on larger doses of colchicine.

Summary

1. Forty-six cases of gout were studied. Fourteen had hypertension and the remaining 32 had normal blood pressure.

2. Evidence is presented that gout is not an aetiological factor in hypertension.

3. There is little evidence that gout causes renal irritation. There is no evidence in our series to support the contention that gout leads to renal lithiasis. Only one case of renal lithiasis was present in our series, and this patient had a stone seven years before the onset of gouty symptoms and has had no recurrent stones since the removal of this one.

4. There is no evidence in this series to support the contention that gout parallels angina pectoris.

5. The value of colchicine as a prophylactic against acute attacks of gout is discussed.

TABLE 2.—GOUT ASSOCIATED WITH NORMAL BLOOD PRESSURE

Case	Age	Duration of disease	Sex	Blood pressure
1	57	10years	M	140/80
2	60	5 ,,	M	124/90
3	53	7 ,,	M	120/80
4	68	20 ,,	M	120/80
5	56	10 ,,	M	114/80
6	42	4 ,,	M	120/80
7	51	5 ,,	M	120/80
8	41	7 ,,	M	136/90
9	45	2 ,,	M	140/80
10	39	13 ,,	M	120/72
11	40	14 ,,	M	120/80
12	45	4 ,,	M	120/80
13	72	40 ,,	M	145/70
14	49	2 ,,	M	120/80
15	49	18 ,,	M	120/90
16	57	1 week	M	140/80
17	55	4 months	M	120/80
18	53	2 years	M	124/80
19	46	7 ,,	M	120/80
20	50	7 weeks	M	120/84
21	49	18 years	M	120/90
22	45	16 ,,	M	140/90
23	47	5 months	M	130/90
24	56	27 years	M	120/70
25	58	3 ,,	M	126/78
26	31	3 months	M	136/76
27	62	27 years	M	130/78
28	48	9 months	M	104/60
29	48	17 years	M	135/90
30	50	20 ,,	M	140/80
31	59	1 year	M	140/80

TABLE 3.—GOUT ASSOCIATED WITH HYPERTENSION

Case	Age	Duration of disease	Sex	Blood pressure
1	51	24 years	M	160/80
2	47	7 months	M	140/110
3	39	3 years	M	140/100
4	61	10 ,,	M	180/100
5	53	6 weeks	F	170/100
6	62	4 years	M	160/86
7	55	2 ,,	M	150/100
8	43	2 ,,	M	145/100
9	69	2 months	M	180/100
10	49	3 weeks	M	150/86
11	50	20 years	M	160/106
12	47	9 ,,	M	190/110
13	39	5 ,,	M	150/120
14	66	10 ,,	M	190/94
15	48	1 month	M	150/80

REFERENCES

Buckley, C. W. (1937). *British Encyclopaedia of Medical Practice*, 6, 45.
—— (1938). *Arthritis, Fibrositis, and Gout*, Lewis, London, p. 130.
Cecil, R. L. (1943). *A Textbook of Medicine*, 6th Edition, Philadelphia, W. B. Saunders Co.
Garcin, R. (1939). *Progrès Med.*, 67, 588–592.
Levine, S. A. (1940). *Clinical Heart Disease*, 2nd Edition, Philadelphia, W. B. Saunders Co.
Lockie, L. M. (1942). "Diagnosis of 'Initial' Attack of Gouty Arthritis," *Clinics*, 1, 571.
——, and Hubbard, R. S. (1935). *J. Amer. Med. Ass.*, 104, 2072.
Master, M., Jaffe, H. L., Dack, S., and Silver, N. (1943). *Amer. Heart J.*, 26, 92.
Meakin, J. (1939). *Practice of Medicine*, 2nd Edition, St. Louis, C. V. Mosby Co.
Osler, W., and McCrae (1925). Osler's *Principles and Practice of Medicine*, 10th Edition, New York, E. Appleton and Co.
Rosenbloom, J. (1918). *J. Amer. Med. Ass.*, 70, 2000.
Stotzer, E. (1939). *Schweiz. med. Wschr.*, 69, 29.
Sydenham, Thomas (1683). "A Treatise of the Gout and Dropsy," published in London May 21, 1683, and quoted in *Medical Classics*, 4, 354, 1940.

NERVE SYMPTOMS IN VERTEBRAL RHEUMATISM

BY

C. W. BUCKLEY

Peripheral nerve symptoms are a common accompaniment of rheumatic diseases of the vertebral column and may be the first, or in the milder cases the only, manifestations. Frequently they are only of minor degree and may be dismissed by the doctor as "a touch of neuritis" and with a few tablets of aspirin; the stage at which treatment of the underlying cause is likely to be most effective is passed before its nature comes to be recognized. This may happen even in cases following an injury, as Walshe (1944) has pointed out, when the symptoms, as in those of rheumatic origin, may be slow and insidious in their development. Numbness often variable in character, sometimes clearing up altogether and then recurring without obvious cause, pins and needles, tingling sensations, and slight muscular weakness, shown perhaps by a tendency to drop things, may be noticed before any actual pain is experienced, which when it occurs may be worse at night and may also be influenced by heat or cold, characteristics which should suggest the possibility of a rheumatic cause. Disseminated sclerosis may be suspected and in the early stages it will be difficult to exclude, unless some rheumatic condition is discovered of a nature and degree adequate to produce the symptoms.

Ankylosing Spondylitis

Babinski reported three cases of lightning pains and loss of tendon reflexes in the lower limbs which gave rise to suspicion of tabes but proved to be due to ankylosing spondylitis; and Garrod (1913) attached importance to these nerve-root symptoms in ankylosing spondylitis, and mentions that some patients who apply for relief from pains of this origin are unconscious of the rigidity of their spines. He made the important observation that they are not due to narrowing of the foramina. Nathan (1916) studied the development of epidural and periradicular exudation in ankylosing spondylitis, and demonstrated that such exudations occurred in the early stages of the disease giving rise to sensory alterations of root distribution. As the inflammatory process subsided a varying amount of fibrosis remained, upon which the severity and permanence of the symptoms depended. These observations are of special interest in view of the fact that pains in the limbs, often fugitive in character but sometimes persistent, and without any obvious changes in the joints, are a feature of the early stages of the adolescent type of ankylosing spondylitis, often occurring for months or years before the appearance of symptoms directly referable to the spinal articulations. Nerve pains are much more frequent in the pre-ankylosing stage than when the spine becomes fixed, especially in the lower limbs, the usual site of onset in the adolescent type being in the lumbo-sacral region. Girdle pains in the lower intercostal region may, however, be due to spondylitis in those cases which while ankylosing in character are not adolescent in time of origin, and in which the maximum bony change in the early stages is in the lower thoracic and upper lumbar region.

Vertebral Osteo-arthritis

While peripheral nerve symptoms are to be met with in ankylosing spondylitis they are much more common in osteo-arthritis of the spine. Garcin and Deparis (1934) studied these nerve lesions especially and describe twelve cases. They point out that muscular atrophy of the Aran-Duchenne type, root atrophy of muscles especially in the leg and thigh, and symptoms indicating syringomyelia, lateral sclerosis, or chronic anterior polio-myelitis, may be set up by irritation and compression of nerve roots in their passage through the spinal foramina. They point out further that radiology in such cases often shows osteophytes in the region of the vertebræ from which the affected nerves emerge but that such lesions may be on the opposite side, and conclude that it is not the formed osteophytes that exert the pressure on the nerve roots but those in course of formation which have not yet undergone changes into bone opaque to x-rays, or to inflammatory or congestive changes of rheumatic nature. At the date of their investigation, however, prolapses of the intervertebral disks had not received the recognition that has been attached to them of late, and it may be that some of the cases for which they offer the explanation referred to may have been cases of this nature.

The nerve symptoms may develop insidiously before obvious osteo-arthritic signs are present or may not appear till long after well-marked spinal osteophytes have been known to exist. They may be apparently induced by some intercurrent illness—influenza or even a common cold. Inflammatory disease in some neighbouring structure may set up local periostitis and thus pressure on the

nerve root in its narrow canal or foramen. Burning or smarting pain is characteristic. The cervical spine seems especially prone to osteo-arthritis owing to the great mobility of this region; the intervertebral disks tend to lose their elasticity and shrink in middle life; this leads to greater play between the vertebral bodies and intermittent strain on the attachment of the muscles and ligaments, which in turn leads to the development of exostoses at their point of attachment. Frequently there is also atrophic change of a degenerative character in the vertebral bodies leading to some degree of collapse and secondary osteo-arthritic changes. As is usually the case in osteo-arthritis, fibrositis may also be present, and the crepitus often experienced in the neck, sometimes audibly, is generally due to fibrositis of the muscle sheaths and tendons and not to the vertebral articulations.

The sixth cervical is the largest of the nerve roots in this region and therefore the most liable to be affected by narrowing of the foramen; in consequence symptoms appear to be most frequently met with in the distribution of the musculo-spiral and median nerves. Careful search for sensory modifications in the area of the nerve roots concerned will help in diagnosis. Gunther and Kerr (1918) made a searching investigation into the nervous disturbances in hypertrophic osteo-arthritis of the spine in patients whose ages ranged from 34 to 72. Their observations upon pain in the region of abdominal organs and in the precordium arising from vertebral causes are of much interest and practical application. They stress the importance of pain, aching, and soreness brought on or aggravated by movement of the spinal column or by actions increasing the intraspinal pressure, such as sneezing or straining, and in all cases cutaneous sensory changes were commonly found. Among other important observations was the association of occipital and sometimes temporal headache with irritation of the first, second, or third cervical nerve roots, and they call attention to the frequency with which headache of this type is attributed to fibrositis of the occipital fascia, often in error. Nachlas (1934) has also described a syndrome of pseudo-angina pectoris originating from demonstrable changes in the cervical spine.

Muscle symptoms are less frequently met with, since actual injury to the nerve fibres interfering with their conductivity, and not mere irritation, is necessary to cause any degree of atrophy. Fibrillation is, however, not uncommon, and atrophy, especially of the small hand-muscles, may occur; it is more liable to be unilateral than bilateral or may vary in degree between the two sides. Atrophy of this type may, however, be reflex in character, and is not uncommon in association, for instance, with osteo-arthritis of the carpal joint of the thumb. Reflexes may be affected and the deep reflexes of the arm should always be tested. Walshe (1944) has laid stress on the importance of unequal affection of the arm jerks as indicating the presence of a local cord lesion such as may result from bony changes in the vertebral canal, or from extrusion of an intervertebral disk.

Radiographic examination should always be carried out; the antero-posterior view is of little value as a rule except to show the presence of supernumerary ribs or abnormalities of the transverse processes, profile views are more useful and the three-quarter profile especially will often reveal obstruction of the foramina which might not otherwise be detected.

Fibrositis

Deep-seated fibrositis in the neighbourhood of the vertebral column may also give rise to peripheral nerve symptoms; this is not uncommon as a cause of sciatic pain, but may also affect the nerve roots in the cervical or dorsal region and give rise to brachialgia or intercostal neuritis. It may be the early stage of spondylitis, and Stockman (1926) states that " ossifying spondylitis " is due to the formation of new bone in chronically inflamed fibrous tissue. This, however, is not usually the case, though it may be noted that Oppenheimer (1938), who has made an extensive study of the various forms of spinal arthritis, stresses the fact that ossification of ligaments is a very common and totally uncharacteristic response to a great variety of intervertebral lesions, inflammatory, destructive, or traumatic. Simple fibrositis, however, with no inherent tendency to develop bony changes, may lead to the formation of exostoses, lipping of the edges of the vertebral bodies, and similar changes, vertebral osteo-arthritis being the end-result.

A case under the observation of the writer illustrates some of these features.

A woman of 50 gave a history of " lumbago " seven years earlier which had never entirely cleared up and had more recently been associated with pain in the left sciatic distribution; x-ray examination of the spine was negative. No infective focus of any kind could be discovered. The pain was chiefly on the left side, was made worse by walking and relieved by lying on that side. She could bend down nearly to touch the toes without pain; the spinal curvatures were normal; treading on any uneven surface caused pain to shoot up the back. She began to experience pain in the left intercostal and pectoral regions which was worse at night, and also pain on tilting the head over to the left side; she felt soreness in the arm with pins and needles sensation in the fingers. The biceps and supinator jerks were normal but the triceps jerk was elicited only with difficulty; the superficial abdominal reflexes were present; cutaneous sensation was normal. X-ray examination showed a very slight degree of lipping of the anterior margins of the vertebral bodies in the lumbar and cervical regions but no thinning of the disks. Her general health was good, there were no indications of cardiac disease, weight was normal for her age. The symptoms improved to some extent with treatment but did not clear up entirely.

There seems little doubt that this was a case of fibrositis of the spinal muscles and ligaments. Pain in the left breast radiating down the arm must always give rise to suspicion of cardiac mischief, but in this case there was no other evidence of that and the history supported a diagnosis of fibrositis.

Diagnosis and Treatment

Peripheral nerve pains, especially if variable in degree of severity or intermittent, should, unless there is an obvious cause, call for radiological examination of that area of the spine from which the nerves are derived. Particularly is this the case in adolescence or early adult life, when they may be due to ankylosing spondylitis. The early recognition of such a condition and its treatment by prolonged rest in bed are of the greatest importance, and it is unfortunate that in so many cases these early premonitory symptoms are disregarded. The sedimentation rate will help in diagnosis, but loss of density in the bones around the sacro-iliac and intervertebral articulations should always arouse suspicion; flattening of the lumbar spinal curve and the characteristic facies and gait may also be early signs. To deal in detail with the treatment of this disease is, however, outside our present scope. In later life special attention should be given in radiological examination to the profile and three-quarter profile views and to evidence of thinning of the intervertebral disks. It must be borne in mind that prolapse of the nucleus pulposus is not limited to the lumbar region but may be equally productive of symptoms in the cervical spine. Operative intervention is less often called for and rest in bed or the wearing of a suitable support for a time may result in relief of the pressure on the nerve root, as is sometimes the case in sciatica due to this condition.

Locally heat is often helpful and moist heat may be found more effective than the various rays which captivate the public imagination. Infra-red rays by their greater penetrative power have some advantages and may be combined with massage, which may be more effective if not too deep and directed rather to improving the local circulation than to breaking down local thickenings, which are not always responsible; very deep pressure may easily do harm. Ionization with histamine followed by light massage is another line of treatment frequently effective in relieving pain. Counter-irritation by the electric cautery may be found useful, and deep x-rays provide a method which has given good results in spondylitis; it is of interest to note that some attribute their effect to counter-irritation, which would justify the use of simpler methods of obtaining this result in the first instance. Manipulation may be successful, but should be attempted only by an orthopædic surgeon. Diathermy is a method which is frequently tried, but the fact that its effect is to raise the temperature of the deeper structures and thus to cause increased circulation and swelling of the tissues under its influence indicates that it may tend to increase the pain rather than give relief; as a preliminary to massage it may be worth a trial, but should not be persisted in unless definite relief is promptly experienced.

References

Garcin, R. and Deparis, M. (1934). *Rev. Méd. Franç.*, **15**, 387.
Garrod, Archibald (1913). *System of Medicine* by Allbutt and Rolleston, London, **3**, 39.
Gunther, L. and Kerr, W. J. (1929). *Arch. Int. Med.* **43**, 212.
Nachlas, I. W. (1934). *J. Amer. Med. Ass.* **103**, 323.
Nathan, P. W. (1916). *Amer. J. Med. Sci.* **152**, 667.
Oppenheimer, A. (1938). *J. Bone Jt. Surg.* **20**, 285.
Stockman, R. (1926). *Edinb. Med. J.*, **33**, 597.
Walshe, F. M. R. (1944). *Lancet*, **2**, 173.

BLOOD PLASMA FIBRINOGEN IN RHEUMATIC AND NON-RHEUMATIC CONDITIONS

BY

A. J. MESTER

A striking feature in many forms of rheumatic disease is the high sedimentation rate of the erythrocytes. The rate of fall of erythrocytes in plasma may be expressed as sedimentation rate (S.R.), or as suspension stability (S.S.). The S.R. (Westergren, Linzenmeier) is expressed by a figure indicating the fall of the column of the red cells in a 200 mm. tube, while the S.S. is expressed as the height of the column of red cells as a percentage, a wider tube being used.

Some Factors in Suspension Stability

The altered S.S. in rheumatic conditions of the joints is characteristic as to both intensity and duration. In the case of rheumatoid arthritis the intensity is significant, because the duration is naturally parallel to the chronicity of this condition. In rheumatic fever the greatly altered intensity is usually of short duration, but it takes a long time before it reaches normal values. Generally we may find an altered sedimentation rate several weeks after complete disappearance of subjective and objective signs and symptoms. The same also applies to the initial stage of rheumatic affections, especially in children, where insignificant, vague complaints may be accompanied by a high sedimentation rate. Thus the insidious character of the rheumatic process may be revealed initially by the altered S.S.

The S.S. is a complicated process, both physically and chemically. Physically it is an outcome of cohesive and repulsive forces acting on the suspended erythrocytes in a viscous fluid medium. The composition of the fluid medium is the most important factor, and the dominant part is played by the blood proteins. The " fastest " protein is fibrinogen, the second " fast " is euglobulin, later pseudoglobulin. The " slow " proteins are the albumins, especially globoglycoid. Clementina M. Gordon and J. R. Wardley have shown that the albumins slow the S.R. globoglycoid more than crystalbumin and seromucoid. The S.R. thus depends on the relative proportions of fibrinogen, globulins, and albumins, and is also affected by the volume of the erythrocytes, therefore the red cell count is important. Although some workers apply a correction for anaemia or polycythaemia, most disregard this factor. In tuberculosis institutions and in rheumatic hospitals, whose patients include a considerable percentage of anaemic conditions due to the basic disease, the correction for anaemia is usually not carried out. Therefore the S.S. method, as described by D. H. Collins *et al.*, in which the estimation of the cell volume of the red blood corpuscles is adopted as a routine, is to be preferred.

In this method the percentage volume of the hypophase—red cell layer—is determined at half-hourly intervals for 2 hours in a 5 c.cm. graduated centrifuge tube, containing 5 c.cm. of venous blood with a minimal amount (1 mg. per 1 ml. blood) of potassium oxalate. The most important is the first hour reading as in Westergren's method, which includes the phase in which the rate of fall of rouleaux is greatest. The simultaneous haematocrit estimation in a 100-mm. long, narrow tube, like Wintrobe's haematocrit tube, gives the percentage volume of the packed red cells (P.C.V.). The S.S. readings are corrected to 42 per cent. cell volume, this value being used as a standard for both men and women. The appropriate correction is added if the C.V. is below 42 per cent. and subtracted if it is above this figure, the magnitude being determined by the difference between 42 per cent. and the observed C.V. The approximate comparative values between S.R. and S.S. are given in Table 1.

Blood Fibrinogen

The importance of the blood fibrinogen in health and disease has received much attention, especially in the liver and the blood, and in rheumatic conditions. Blood fibrinogen is thought to come from the liver. Some authors believe that a certain amount may be held in reserve in the intestinal tract. Fibrinogen constitutes 3–6 per cent. of the total blood proteins, representing 250–400 mg. per 100 ml. plasma. It is the most labile protein in the blood; it regenerates very quickly (in a few hours) as opposed to other blood proteins, which re-

TABLE 1

APPROXIMATE COMPARATIVE VALUES FOR S.R. AND S.S.

Westergren*	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160	170	180	190	Westergren
S.S.†	95	90	85	80	75	70	65	60	55	50	45	40	35	30	25	20	15	10	5	S.S.

* Height of column of supernatant plasma.

† Being the height of the column of red cells as a percentage.

generate more slowly. The quick response of blood fibrinogen to infections, intoxications, and tissue destruction takes place in persons whose liver cells are not extensively damaged. In severe damage of the liver, as in phosphorus or chloroform poisoning, the blood fibrinogen quickly, sometimes in few hours, drops to very low level. It returns to normal values only in case of regeneration of the liver cells. In severe primary anaemias, in leukaemias, in haemolytic jaundice, and in banal icterus the blood fibrinogen is low. In the fasting state and when the diet is uniform, the blood fibrinogen maintains a fairly stable level, and in health the physiological blood-fibrinogen fluctuations are small. In the presence of an infection, intoxication, or any condition causing tissue destruction, an increase in blood fibrinogen will soon occur in an individual with a healthy liver even with a slight secondary anaemia. According to Kisch a two-fold connexion exists between the blood fibrinogen and the reticulo-endothelial system (R.E.S.). (1) The R.E.S. is supposed to produce the material for the fibrinogen. (2) Extensive damage to liver cells impairs the fibrinogen production. The important rôle of the blood fibrinogen in the mechanism of blood clotting is known.

Because of the changes in sedimentation rate in rheumatic diseases it seemed desirable to investigate the fibrinogen values in the different types. Two points may first be noted: (1) In the early stage of acute rheumatism and rheumatoid arthritis there is to be found in the affected parts a great mass of precipitated fibrin and fibrinoid substances—Klinge's "*fibrinoide Verquellung*." (2) The predominant rôle of the fibrinogen in the S.R. The marked alteration in the sedimentation rate in rheumatic fever and rheumatoid arthritis, non-purulent diseases, deserves special attention. A satisfactory explanation of the increased fibrinogen production in rheumatic fever and in rheumatoid arthritis is not yet forthcoming. The rheumatic agent may so affect the liver as to stimulate the production of fibrinogen without reaching a stage which would depress this function; or it may be that in rheumatic joint conditions the extent of tissue destruction is great; or some individuals may be predisposed to an abnormal production of fibrinogen, reacting to a supposed specific or nonspecific agent, and thus be prone to rheumatic joint conditions?

Present Investigation

In an attempt to throw light on these problems, the blood fibrinogen, the suspension stability, and the packed red cell volume were estimated in 220 patients attending the Devonshire Royal Hospital. The blood plasma fibrinogen was estimated by the gravimetric method of Cullen-van Slyke in 2 ml. of plasma, and the results recorded are ash-free fibrinogen in mg. per 100 ml. plasma. This method gives as a normal value 250–400 mg. per 100 ml. The S.S. and hematocrit estimations were made by the method of Collins *et al.* These 220 patients comprise:

Rheumatoid arthritis, 53.
Spondylarthritis ankylopoietica, 10.
Osteoarthritis, 37.
Subacute rheumatism, 20.
Chronic muscular rheumatism, 38.
Traumatic arthritis, 13.
Traumatic muscular affections, 12.
Chronic articular gout, 10.
Static conditions (flat feet), 5.
Endocrinogenic and hyperpietic polyalgiae, panniculitis, 7.
Sciatica, 7.
Unclassified conditions, 8.

TABLE 2

RHEUMATOID ARTHRITIS

Mean of Fifty-Three Cases

Suspension stability	Packed cell volume	Corrected S.S.	Fibrinogen mg. per 100 ml.
64	37	71	520

Statistical Correction for Fibrinogen

Mean	Range	Standard deviation	Coefficient of variation	Standard error of S.D.	Probable error
520	340 to 700	83·24	16·00	8·08	5·44

SPONDYLITIS ANKYLOPOIETICA

Mean of Ten Cases

Suspension stability	Packed cell volume	Corrected S.S.	Fibrinogen, mg. per 100 ml.
70·7	43·6	68·4	559

Statistical Correction for Fibrinogen

Mean	Range	Standard deviation	Coefficient of variation	Standard error	Probable error
559	460 to 700	86·42	15·46	24·33	16·41

OSTEO-ARTHRITIS

Mean of Thirty-Seven Cases

Suspension stability	Packed cell volume	Corrected S.S.	Fibrinogen, mg. per 100 ml.
77·5	41·6	78	381

Statistical Correction for Fibrinogen

Mean	Range	Standard deviation	Coefficient of variation	Standard error	Probable error
381	220 to 580	76·93	20·18	14·50	9·77

SUBACUTE RHEUMATISM

Mean of Twenty Cases

S.S.	P.C.V.	Corrected S.S.	Fibrinogen mg. per 100 ml.
77·6	41·7	78	413·5

Statistical Correction for Fibrinogen

Mean	Range	S.D.	C. of F.	S.E.	P.E.
413·5	230–670	69·64	16·83	11·04	7·44

CHRONIC MUSCULAR RHEUMATISM

Mean of Thirty-Eight Cases

Suspension stability	Packed cell volume	Corrected S.S.	Fibrinogen, mg. per 100 ml.
87	43	86	448·85

Statistical Correction for Fibrinogen

Mean	Range	Standard deviation	Coefficient of variation	Standard error	Probable error
448·85	370–570	48·64	10·85	5·58	3·76

TRAUMATIC MUSCLE AFFECTIONS

Mean of Twelve Cases

Suspension stability	Packed cell volume	Corrected S.S.	Fibrinogen, mg. per 100 ml.
92·5	42	92	345·7

CHRONIC GOUT

Mean of Ten Cases

Suspension stability	Packed cell volume	Corrected S.S.	Fibrinogen, mg. per 100 ml.	Blood uric acid, mg. per 100 c.c.
72·4	43·7	69·1	466	5·43

Discussion

SPONDYLARTHRITIS ANKYLOPOIETICA

The plasma fibrinogen value in this disease affecting young men, is higher than in rheumatoid arthritis, —559 mg. as compared with 520 mg. mean—but the difference is " not significant."

Osteoarthritis

In pure uncomplicated cases the S.S. and blood fibrinogen are within normal limits but some patients show both lowered S.S. and increased fibrinogen. This may be attributed to several complications: it may be a banal, ordinary inflammation from small infractions as a result of microtraumata in one or more affected joints (e.g. bilateral osteoarthritis of the hip-joints, or a superimposition of rheumatoid arthritis; or vice versa it may be a superimposed osteoarthritic process on a still active rheumatoid process. Complicated cases of osteoarthritis of this kind are not infrequently met with.

Subacute Rheumatism

Patients in this group show great variety in the activity of the disease: some have had only one attack as far as 14 years back, while others have had relapses recently. Hence the great standard deviation. All these patients have rheumatic heart disease.

Chronic Muscular Rheumatism

In this group the most striking results were found: an increased blood fibrinogen in patients with normal S.S.; the mean for fibrinogen being 448·85 mg. per 100 ml. plasma, with a probable error of 3·76, is definitely increased. The diagnosis of chronic muscular rheumatism was based not only on the history given by the patient, but also clinically by the presence of objective signs and symptoms. The statements of the patients were carefully scrutinised and the reliability checked. On examination objective signs were found such as muscle thickenings, circumscribed and well-defined areas of tenderness or muscle spasm, etc. The fact that in these patients the blood fibrinogen is increased where the S.S. is normal deserves to be stressed, as such a discrepancy was not found in any other condition here discussed. This discrepancy may throw some light on the nature of chronic muscular rheumatism, because, after careful exclusion of other possible factors leading to an increased blood fibrinogen, it supports the belief of English clinicians as to the rheumatic aetiology of chronic muscular ailments. There are, of course, muscular pains of a different aetiology, as gout, gonorrhoea, etc., but these represent a small fraction in the number of chronic muscular sufferers, and this aetiology will be detected in the course of careful examination.

If a rheumatic aetiology for these chronic muscular affections is accepted, gold treatment might be adopted as a natural corollary. Taking into consideration the leniency of the process both in the clinical picture and in the biological findings, I would suggest small doses of gold, both for each individual dose and for the whole course. Having diagnosed chronic muscular rheumatism in cases in which these are no contraindications (skin, kidney, liver affections, etc.) I adopt as the initial dose 0·005 g. of a gold compound containing approximately 50 per cent. metallic gold in watery solution (myocrisin) and increasing slowly to 0·05 g. for a dose in 7-days' intervals, the total for a course being 0·25 of gold salt—i.e. 0·125 g. of gold.

This phenomenon of a normal S.S. with a raised blood fibrinogen in chronic muscular rheumatism may be due to the interplay of other factors determining the S.S., possibly inhibition by albumins, or perhaps due to the tissue reactivity of the muscles.

Chronic Articular Gout

The patients in the active stage show a low S.S. and increased blood fibrinogen. All these patients have had increased blood uric acid. The clinical and radiological findings were in conformity with the diagnosis.

Sciatica

This may be also of rheumatic aetiology, although probably only in a small percentage, but the number of observations was too small to allow any conclusions being drawn.

Other Conditions

Traumatic joint-and-muscle affections, static conditions (flat feet), endocrinogenic disseminated pains —all show uniformly a normal S.S. with a normal blood fibrinogen.

Conclusions

The blood fibrinogen estimations may be of additional diagnostic value in cases of rheumatic conditions, especially in chronic muscular rheumatism, when the S.S. is normal. The active rheumatic affections of joints and muscles in patients with a healthy liver and normal blood, or only with slight secondary anaemia, provoke an increased blood fibrinogen. The increased blood fibrinogen with normal S.S. in chronic muscular rheumatism presents an indication for gold treatment in low doses. There is not sufficient evidence to support the view that liver function is impaired in rheumatic sufferers, their response to the fibrinogen-creating stimulus being normal.

I desire to express my indebtedness to Dr. C. W. Buckley for his suggestions and to Mr. Joseph Race, biochemist to the Devonshire Royal Hospital, for much valuable help and kindness.

I would also express my appreciation to the Polish Board of Education for a grant.

References

Buckley, C. W. (1938). *Arthritis, Fibrositis, and Gout*, H. K. Lewis & Co., London.
Collins, D. H., Gibson, H. J., Race, J., and Salt, G.B. (1939). *Ann. rheumat. Dis.*, **1**, 333.
Foster, D. P., and Whipple, G. H. (1922). *Amer. J. Physiol.*, **58**, 379 and 393, 407.
Gordon, Clementina, M., and Wardley, J. R. (1943). *Biochem. J.*, **7**, 393.
Isaac-Krieger, K., and Hiege, A. (1923). *Klin. Wschr.*, **2**, 1067.
Kisch, F. (1923). *Klin. Wschr.*, **2**, 1452.
McLester, J. S. (1922). *J. Amer. Med. Ass.*, **79**, 17.
Ponder Eric. Hematocrit Method.
—— (1944). Sedimentation in The Year Book Pblrs. Inc. Chicago, Year Book of Physical Medicine, pp. 597, 1408.
Race, J. (1929). *Proc. Roy. Soc. Med.*, **22**, 611.

RHEUMATIC DISEASE IN THE MIDDLE EAST

BY

G. D. KERSLEY

A war will sometimes produce the opportunity for obtaining figures, not normally available, of the incidence of a disease and its reactions under varying conditions of climate and strain.

Facts that may have any bearing on the aetiology or classification of the rheumatic diseases are badly needed, and with this end in view an effort was made to analyse figures of morbidity among our troops in the Middle East. In order to obtain information on the number of different types of rheumatism occurring in a healthy population of young adults, under different seasonal and climatic conditions, the reports of all hospitals were carefully analysed over the period of some twelve months. In assessing the effect of climate, however, such figures have to be treated with caution owing to the movement of troops from one country to another within the Command, and in consideration of the fact that in some countries, such as Palestine, there were included among the admission records a number of local enlistments, whose psychology has to be borne in mind in assessing the exactitude of diagnosis wherever this rested on clinical history rather than on unmistakable physical signs.

Incidence

For the purpose of this investigation, under the heading of rheumatic diseases were included all cases of arthritis, fibrositis, and sciatica admitted to any hospital in Egypt, Palestine, Syria, Tripolitania, or Malta for either investigation or treatment. In the period under review there were 1,288 cases in this group, which comprised 2·5 per cent. of all medical admissions. In Palestine and Syria, where the winter and early spring is in many places very wet and cold, the incidence was a little higher (2·9 per cent.), and in Egypt, with its temperate winter, hot dry early summer, and humid autumn, the incidence was 2·2 per cent. The highest seasonal incidence—namely, 5·1 per cent.—was in the first quarter of the year, dropping to 3·2 per cent. between April and June, to 1·9 per cent. between July and September, and rising a little to 2·6 per cent. in the last quarter of the year.

Types of Disease

The sub-division of rheumatic cases into clinical syndromes on the basis of the reports was possible in only 775 of the cases. Of these, 33 per cent. could be classed as muscular fibrositis, 32 per cent. as acute joint conditions, 21 per cent. as chronic arthritis, and 14 per cent. as sciatic pain. Of these syndromes, the differential diagnosis and aetiology of the acute joint conditions in particular presented interesting problems, raising the question both of the inter-relationship of acute rheumatic fever in adults to other forms of rheumatism, and also of the virus factor in aetiology. Bearing on the first problem, Ferguson (1943), in a review of 243 cases of acute arthritis of the same age group in the Canadian Army, found that in 58 per cent. symptoms began within12 weeks of an acute streptococcal infection, and that in 71 per cent. of these, symptoms occurred within 2 weeks and in 95 per cent. within 4 weeks of its onset. Twenty per cent. gave a past history of rheumatic fever, 27 per cent. eventually developed cardiac lesions thought to be rheumatic, and 6 per cent. progressed to a chronic rheumatoid syndrome. He stated that 71 per cent. re-acted favourably to salicylates, and that many of the remainder had never received full doses of this drug. His findings, therefore, bear out the suggestion that one large group of cases are suffering from the adult form of acute rheumatic fever.

In addition to this acute form of adult rheumatism, there exists a subacute, more insidious type, corresponding to the subacute rheumatism of childhood. These cases again often give a past history of rheumatic fever and sometimes show signs of a valvular lesion. They complain of aching in certain joints, especially the wrists and elbows, symptoms coming on most frequently two weeks after a nasal or tonsillar infection. There is often a little transient swelling and there may be signs of re-activation of an old carditis. The sedimentation rate is normal or only slightly raised, the course is chronic, and the results of treatment, including that obtained by the exhibition of salicylates, are far from dramatic. Of 13 cases followed up for a period of 5 years, one developed a polyarthritis, 4 still had periodic attacks of arthralgia, 2 had a slightly swollen joint at the time of review, and 6 considered themselves completely cured (Kersley, 1939). Out of this small group of " subacute rheumatic infections," at first clinically indistinguishable, emerges a case of true arthritis, others that could justifiably be diagnosed as peri-articular fibrositis, yet some at least were undoubtedly of the same aetiology as juvenile rheumatism.

Other types of arthritis that must be considered in differential diagnosis, in addition to those due to well-defined specific infections such as gonorrhoea

and to juvenile gout, are acute osteo-arthritis; a multiple arthritis of the small joints with absence of constitutional debility or trophic changes in the skin, and with a normal or only slightly raised sedimentation rate; palindromic rheumatism, rare in this country, but described by Hench and Rosenberg (1941) as a syndrome of transient attacks of pain, swelling and redness of one or more joints in adults of either sex, recurrent over a period of many years, and accompanied by no constitutional, blood, or x-ray changes; and the arthritis accompanying non-specific urethritis. This latter condition brings us to the second question—that of a virus factor in aetiology.

The Infective Factor

Van Rooyen believes that those cases with acute arthritis following non-specific urethritis and usually associated with some iritis or conjunctivitis, a syndrome not uncommon in the Middle East, were caused by infection with the Waelsch virus, also responsible for swimming-bath conjunctivitis, and inclusion urethritis and cervicitis. For these latter conditions the incubation period is stated to be 6–10 days. More work, however, is required, including the examination of urethral scrapings and the carrying out of Frei antigen tests, to prove or disprove this hypothesis. Corroborative evidence for this theory was afforded by Eagles *et al.* (1937), who described the presence of inclusion bodies in the pericardium and joints of children dying from rheumatic fever. When, however, the present evidence for a virus is weighed against that for a streptococcal origin it carries little weight unless the effect of symbiosis is remembered.

The work of Rosenow (1923), who showed that two-thirds of a series of rheumatic subjects had their rheumatic state re-activated by an epidemic of haemolytic streptococcal infection, but were not affected in this way by infections with other types of organism, of Coburn (1931), who demonstrated that exacerbations of rheumatism in children could be stopped by their transference to a climate which caused the disappearance of streptococci from the flora of the nasopharynx, of Collis (1939) who carried out cultural examinations post mortem on tonsillar tissue, and of Green (1939), who obtained a similar result from hearts from rheumatic fever cases, leaves little doubt that the streptococcus plays some part in the causation of rheumatic fever.

Similarly, the blood and joint culture work of Cecil (1929) and Gray (1932), though disputed by some, when backed by the agglutination and skin sensitivity tests of Keefer (1933), produce strong evidence that there is some similar factor in many cases of rheumatoid arthritis. The evidence in all these cases, however, is not completely convincing in itself: two other factors require consideration—that of allergy or sensitization, and that a virus may be necessary in symbiosis with the causative bacterium in order to produce the clinical syndrome of rheumatism. The question of tissue sensitization is too large a subject to embark on here, but the incubation period between evidence of infection and rheumatic symptoms, the results of skin sensitization tests, and the experimental work on immune body response in rheumatic subjects all suggest that allergy will be found to play a part in the jig-saw puzzle.

The most recent experimental work throwing light on the symbiosis theory is that of Gordon (1939), who produced arthritis in rabbits by the combined intravenous injection of a streptococcus and M4 virus—neither producing the condition by themselves when used in the same dosage and only the virus being recoverable from the tissues. May not the need for a similar symbiosis between a virus and certain bacteria be responsible for the difficulties in interpreting results of many experiments based on the conception that rheumatism is due to a specific bacterium, for the difficulty in obtaining a specific bacterium from the tissues in 100 per cent. of cases in one particular type of rheumatic disease, for the results of the transmission experiments recorded by Copeman (1944), for the way in which cases of non-specific urethritis develop arthritis, and for the relapse which frequently occurs (Kersley 1942) when patients suffering from a non-specific type of rheumatism become infected with gonorrhoea?

Much more research combined with clinical observation is necessary before we can interpret all the facts; but the conception of the triad, (*a*) bacterial infection, probably non-specific; (*b*) virus in symbiosis; and (*c*) tissue sensitization, opens up a huge field for future investigation.

Summary and Conclusions

Some figures concerning the seasonal incidence of rheumatic disease among our Forces in different countries in the Middle East have been given.

Evidence bearing on theories of a virus or virus and bacterial causation of rheumatism are discussed, together with views on the relationship of the rheumatic syndromes seen among young adults to those found in children.

References

Cecil, R. L., Nicholls, E. E., and Stainsbury, W. J. (1929). *J. Exper. Med.*, **50**, 617.
Coburn, A. F. (1931). *The Factor of Infection in the Rheumatic State*, Baltimore.
Copeman, W. S. C. (1944). *Ann. Rheum. Dis.*, **4**, 37.
Collis, W. R. F. (1939). *Lancet*, **2**, 817.
Eagles, G. H. *et al.* (1937). *Lancet*, **2**, 421.
Ferguson, G. C. (1943). *Canad. Med. Ass. J.*, **49**, 492.
Gordon, M. H. (1939). *Ann. Rheum. Dis.*, **1**, 5.
Green, C. A. (1939). *J. Roy. Nav. Med. Serv.*, **25**, 218.
Gray, J. W. *et al.* (1932). *Texas State J. of Med.*, **28**, 203.
Hench, P. S., and Rosenberg, E. F. (1941). *J. Amer. Med. Ass.*, **117**, 1560.
Keefer, C. S., *et al.* (1933). *J. Clin. Invest.*, **12**, 267.
Kersley, G. D. (1942). *Proc. Roy. Soc. Med.*, **35**, 653.
—— (1939). *J. Roy. Inst. Pub. Hlth.*, **2**, 101.
Rosenow, E. C. (1923). *Amer. Med. J. of Dis. Child.*, **26**, 223.
van Rooyen, C. E., and Rhodes, A. J. (1940). (*Virus Diseases in Man*, London.

"A.C.B. SERUM" OF PROF. BOGOMOLETZ IN THE TREATMENT OF RHEUMATISM

BY

FRANCIS BACH

In the *British Medical Journal* of Aug. 14, 1943 (p. 203), Prof. Bogomoletz published an article in which he claimed that he had produced a serum the use of which caused considerable amelioration both of symptoms and of pathological tissue changes in "rheumatism." The Empire Rheumatism Council invited Prof. Bogomoletz to send some of this serum to this country in order that it might be tested upon patients here, and he readily acceded to this request. The Empire Rheumatism Council is now able to give an account of the trial of the serum.

Theoretical Considerations

Prof. Bogomoletz bases his treatment on his conception of the "physiological system of the connective tissue" described in his book *Constitution and Mesenchyme*. He stimulates the connective tissues by the use of a "cytotoxic serum." The principle underlying the treatment is to use the recipient's tissues as antigens. The serum is produced by the immunization of horses with the cells of the spleen and bone-marrow taken from a human corpse, preferably of a person who has died a sudden death. The antibodies thus produced are capable of "blocking" or "stimulating" the reticulo-endothelial tissue of the recipient. The cellular elements of the reticulo-endothelial system produce various chemical substances which form the "haemato-parenchymal barrier," which Prof. Bogomoletz pictures as not only a barrier but a depot for various nutritive substances where the cells obtain the necessary "energetic and plastic resources." Upon the condition of this barrier depends the condition of the cells of the parenchyme, which he holds responsible for the general reactivity of the individual and his health and longevity. The substances which stimulate this system are present in the spleen and lymphatic nodes; they are "autocatalizators." For therapeutic purposes sera which give a complement fixation in a dilution of not less than 1 in 100 are found most suitable. The serum is injected at body temperature into the patient subcutaneously, the dose being 0·03–0·10 c.cm. diluted ten times with an isotonic solution of sodium chloride. Three injections are given at 2–3 day intervals; the last injection must be given not more than 10 days after the first. Prof. Bogomoletz claims that clinical experience has shown that this serum given in such doses has a strong stimulating effect on the cellular elements of the "physiological system of the connective tissue." In large doses the serum has an inhibiting influence on these tissues.

Physiological Action

The mechanism of the stimulating action of A.C.B. serum is shown in a series of phenomena which occur within a few hours or days of its injection. The first change to be noted usually follows the second injection. This is an increase in the permeability of the haemato-parenchymal barrier, a dilatation of the capillaries, and a significant relative lymphocytosis. The latter disappears within four hours and is replaced by a relative monocytosis, and an increase in the number of adult segmented neutrophils which may remain for a few days. The amount of complement in the blood and the opsonic index are increased. The blood sedimentation rate when raised falls, and when low increases. There is a tendency for it to return to normal. The purpose of the serum is to intensify immunity. It acts not directly on micro-organisms or their toxins but on the "reactivity of the physiological system of the connective tissue," the condition of which determines the destruction of pathogenic organisms and their toxins.

Present Investigation

It has been claimed that this is a valuable and successful method for the treatment of "rheumatism." Many people suffering from a variety of conditions diagnosed or labelled "rheumatism" or "arthritis" have asked their doctors about this new treatment. A careful review of the literature sent with the serum gives little indication as to the type of rheumatism, or the stage in the arthritic process at which the serum should be employed. It was thought advisable to take for study patients whose ill-health had been carefully investigated from the clinical, laboratory, and radiographic aspects, and who could be classified under one or other of the recognized types of rheumatism.

Forty-eight patients in all have been investigated, as in-patients 32, as out-patients 16. They fall into the following clinical groups, using the Royal College of Physicians' classification:

Rheumatic Fever	2
Rheumatoid type of Arthritis	35
Spondylitis Ankylopoietica..	2
Gonorrheal Arthritis	1
Osteo-arthritic type:	
(i) Hip and lumbar arthritis 1	2
(ii) Fingers (Herberden's nodes) 1 ..	
Non-articular Rheumatism:	
(i) Diffuse muscle pains 3	6
(ii) Lumbago and sciatica 3	
	48

Clinical improvement was assessed on subjective features such as "feeling better," "less stiff," "eating and sleeping better," and on objective features such as a noticeable reduction in muscle spasm and joint swelling, a gain in weight, a return to normal of a raised temperature, and a fall in the sedimentation rate. In the main, when improvement occurred it was noted mainly in the subjective rather than the objective state. Clinical improvement was observed in fourteen: definite in 7; and slight in 7.

Of those who showed definite improvement, the type of disease was: rheumatoid arthritis in 3; rheumatic fever in 1; gonorrheal arthritis in 1; spondylitis ankylopoietica in 1; muscular rheumatism in 1.

It is interesting to note that of the three rheumatoid arthritis who showed definite improvement, two were tired Lambeth women with advanced active rheumatoid arthritis who were admitted from an out-patients department in London into a Sector hospital outside London for a rest and were given the serum immediately. Pain was relieved, the joints became less swollen, and the blood sedimentation rate remained unchanged. They re-remained in hospital a month. Two months later they had relapsed; one of them is again in hospital, her joints more swollen and painful than on her first admission. The third case was one of inactive rheumatoid arthritis in a young woman in whose symptomatology there was a very marked psychological factor. Two months after her discharge her symptoms had returned and were relieved by two injections of sterile water. The patient with muscular rheumatism, improving markedly, had a haemolytic streptococcal injection of the throat, with a raised sedimentation rate. The pain and swelling subsided and the streptococcus disappeared from the throat, and the sedimentation rate, which was high, returned to the upper normal limit. When re-examined two months later she was quite well, "felt better than she had for years," and the sedimentation rate was normal.

One of the two rheumatic fever cases improved considerably while under treatment, the joint swelling subsided, temperature and sedimentation rate returned to normal. It is hard to judge the extent to which the clinical picture and natural course of the disease in this case and in that of the acute gonorrheal arthritis were modified by the serum injections. The young man suffering from spondylitis ankylopoietica said that he felt better, but there was improvement neither in his chest expansion nor in the hip movements, and his sedimentation rate remained raised and unchanged.

Four of the patients with rheumatoid arthritis were referred by the Soviet Embassy. After the first course of treatment, three of these stated they were much better. At the end of the second course these three had unfortunately relapsed and said they had derived no benefit from the treatment. Two months later their condition was unchanged. They were patients in an advanced stage of rheumatoid arthritis who had come expecting a great deal from the new treatment.

The duration of each course of treatment was 7–10 days. The patients have now been under review for four to five months. All have been re-examined two months after their last injection. In 25 patients a diffuse and painful rash appeared at the site of the injection on the day after the second or third dose, and lasted for two or three days. In some cases the rash was quite mild; in others there was a circular patch, 3–4 inches in diameter, localized at the site of the injection. This was the only unpleasant reaction that was observed during the treatment.

The temperature of three patients was raised at the onset of treatment; at the end of a course of injections the temperature returned to normal in two of them. The first was a young man with rheumatic fever, temperature varying between 99–100° F. for a week before giving A.C.B. serum. The second was a young woman with arthralgia and a low-grade pyrexia in whom haemolytic streptococci were grown from the throat. The third was a middle-aged man suffering from rheumatoid arthritis in an advanced and active phase. The raised temperature was slightly less marked after the treatment.

In the rest of the series, the temperature was normal.

Blood Changes.—The blood sedimentation rate varied from 1 mm. to 118 mm. at the end of the first hour (Westergren). In some cases the sedimentation rate increased; in some it decreased; and in others it remained unchanged after one or two courses of injections. In those in whom clinical improvement was noted, it appeared to bear no relation to the height or change in the blood sedimentation rate.

Of the patients suffering from the rheumatoid type of arthritis who claimed definite improvement the blood sedimentation rate was within normal limits in one, out of three. In two out of the three it was raised, and was unchanged after the serum. In both the rheumatic fever cases the sedimentation rate was raised and after treatment it gradually returned to normal in the one case, but in the other it remained raised.

A differential blood count was done in some cases, but this showed no marked changes. For example, Mrs. P. was suffering from rheumatoid arthritis:

Date	R.B.C. Erythro-cytes	Hb. Haemoglobin	C.I.	Leucocytes					S.R. Westergren
				Neutros.	Eosinos.	Basos.	Lymphos.	Monos.	
19.4.44	5,040,000	12·7 g. per cent. (92 per cent. acid haematin)	0·92	16,750–9,390	334	331	5,682	1,010	55
28.4.44	5,320,000	11·32 g. per cent. (82 per cent. ac. Hn.)	0·77	10,050–6,128	100	Nil.	3,118	701	62
15.5.44	5,420,000	11·59 g. per cent. (82 per cent. ac. Hn.)	0·78	13,450–10,220	Nil.	Nil.	2,693	537	70

Comments

This preliminary investigation does not support a claim that the A.C.B. serum can be considered as a "cure for rheumatism." That assessment of any method of treating the various disorders included in the term "rheumatism" is difficult has been shown by the results published of trials carried out in recent years in this country, the U.S.A., and on the Continent, with vaccines, gold preparations, vitamins, local injections, and so on. It is even more difficult to evaluate methods which are claimed to have a constitutional effect than those which merely offer to relieve pain or joint swelling. Although the rationale of gold treatment is not as yet clearly understood, many clinicians have claimed improvement in the general health of the rheumatic patient by its use, and this may well raise the hypothesis that by acting on the reticulo-endothelial system the resistance of the individual may be increased and the rheumatic process modified.

Prof. Bogomoletz and those Russian clinicians who have claimed success with the A.C.B. serum in the literature at our disposal neither define the type of "rheumatism" most amenable to benefit, nor give details of the range of dosage to be employed. It is possible, and even probable, that the type of case and the stage in the pathological process that has been used for this preliminary survey are not those which Prof. Bogomoletz would himself have chosen. It is hoped that more detailed information will be given at some future date, so that a clinical and laboratory investigation on certain carefully selected groups of patients may be carried out, and results obtained which would justify the claims which have been made for the A.C.B. serum. The results of this preliminary investigation do not justify a favourable verdict.

It gives me great pleasure to acknowledge the help and encouragement which Lord Horder has given me throughout this investigation and in the preparation of this Report.

The foregoing article was submitted to the Empire Rheumatism Council as a report on the tests which had been made. Mr. Paul Winterton, the Moscow correspondent of the *News Chronicle* received a copy of the report and approached Professor Bogolometz, who informed him that it was now his opinion that the serum is suitable for the cure of rheumatism only in the acute phase of the illness. Academician Nikolai Strozhesko, in whose clinic the action of the serum in rheumatism was studied, writes that the serum in stimulating doses produces the best effect with infectious diseases in the second (allergic) period of their course. In chronic rheumatism (chronic arthritis and endocarditis) the serum should not be used.

BOOK REVIEW

Pathology and Therapy of Rheumatic Fever. By Leopold Lichtwitz, M. D., late Chief of the Medical Division of Montefiore Hospital and Clinical Professor of Medicine at Columbia University, with a foreword by William J. Maloney, M.D. Grune and Stratton, New York, 1944, 225 pp., 69 illustrations. Price $4.75.

This interesting volume, published shortly after the author's death, presents an extensive and broadly-conceived study of the problem of rheumatic fever as it is seen from the point of view of those who hold this disease to be a manifestation of an allergic sensitization of the mesenchyme to known or unknown antigens. In this respect the book is a special plea for a particular thesis regarding the aetiology of rheumatic fever. It is not a complete review of the rheumatic fever problem. As thus conceived, the book is brilliantly written. In it a great many aspects of rheumatic fever are discussed lucidly and intelligently in the light of the author's masterful experience of internal medicine, and against the background of a wide acquaintance with American and European literature.

In addition to the classic manifestations of rheumatic fever, Lichtwitz and many other followers of the allergic hypothesis consider the rheumatic state to include many conditions such as fibrositis, dermatomyositis, rheumatoid arthritis, Still's disease, scleroderma, and disseminated lupus erythematosus. Even certain chronic ulcers of the legs, epidemic pleurodynia, phlebitis migrans, and many other poorly-understood diseases are looked upon as forms of rheumatic fever. The clinical features of many of these, as well as considerations concerning their possible pathogenesis, are discussed in the book. An attempt is made to define the characteristics of the musculo-skeletal diseases which are excluded from this rheumatic category.

Briefly summarized, the allergic hypothesis of rheumatic fever as described by Lichtwitz holds that the rheumatic disease results when an individual with sensitized mesenchyme is exposed to an offending antigen. In most instances this antigen is the product of bacterial growth, but it may be some other foreign protein substance or even certain non-protein chemical toxins. No constitutional type is looked upon as immune to rheumatic sensitization, but those who are most prone to it are said to be the young and asthenic persons with an " inferior " mesenchyme as evidenced by certain stigmata. These include an infantile body form, blue sclerotics, disturbances of growth, or softness of the cartilages of the nose and ears. These persons are said to suffer frequently from autonomic imbalance, which is seemingly defined as an increased tendency to local or general sweating, clammy hands, and a positive oculo-cardiac reflex. The rheumatic " shock organ " is not the same in every person: in some it is predominantly the heart; but it may be articular, dermal, neural, or muscular organs in others, and frequently a number of these are affected in the same individual. In every instance the rheumatic " shock organ " is some structure which exists in identical form on both sides of the body, and the rheumatic lesion is defined as a bilaterally symmetrical allergic reaction appearing anywhere in the body.

The character of the rheumatic reaction is quite variable, being influenced by a number of known and probably by many unknown factors. Nervous impulses from the brain stem, climatic, occupational, economic and hereditary influences—all may shape the nature of the rheumatic fever in a particular individual. Sometimes the rheumatic inflammation is brief, terminating in complete healing. In an individual with inadequate defence, however, the reaction may be " anergic "—that is, weak. For example, an anergic form of arthritis would be one associated with atrophy, osteoporosis, and even cyst formation. If the defence is strong the course of the arthritis, though equally unfavourable, may be characterized by a different reaction, possibly by overgrowth of the synovial tissues with much pannus formation and possibly ankylosis. Such an exuberant reaction is designated " hyperergic." All rheumatic diseases may be analysed in this manner as " plus-minus " reactions in various shock organs.

Unfortunately many of the data marshalled in support of the central idea of this book are not appraised critically or scientifically. Professor Lichtwitz has stated the case for the allergic hypothesis with considerable eloquence, but many of his views on this subject are nevertheless highly speculative. The reader will need to be constantly aware of this, for, in spite of the fact that a casual reading of this book may give a contrary impression, dispassionate inquiry reveals that no final estimate can be reached at this time concerning the part allergy may play in rheumatic fever.

This book is recommended as a provocative and stimulating intellectual experience for physicians who are interested in rheumatic fever.

EDWARD F. ROSENBERG.

EMPIRE RHEUMATISM COUNCIL

EIGHTH ANNUAL REPORT

NOVEMBER, 1943, TO NOVEMBER, 1944

My Lords, Ladies, and Gentlemen,

You will cordially welcome the intimation from St. James's Palace that H.R.H. the Duke of Gloucester wishes to continue as our President during his term of office as Governor-General of Australia. The letter stated: "Absence overseas will in no way diminish His Royal Highness's interest in the Council's work, which he is encouraged to know has been carried on, despite war-time difficulties, to a stage of hopeful promise."

Considerable attention has been given during the year by your War Emergency Committee to the matter of the post-war organization of our work. Up to August last hope was entertained that it would be possible to summon the Annual General Meeting in November, 1944, and to ask members to reconstitute the various Standing Committees, sessions of which were suspended in 1939. But at a meeting of the War Emergency Committee held on August 23rd it was unanimously decided that this was impracticable, and it was agreed that an Extraordinary General Meeting should be summoned as early in 1945 as the development of the war allowed. This decision was regretted, as our Emergency Executive Committee (though including representatives of all the chief standing committees and thus reflecting the general view of the Council) is sensible of the loss of the re-invigorating influence of meeting its constituents and learning by discussion their views as to the best conduct of our campaign. It was, however, unavoidable as well as regrettable. When next they meet, members will expect to have before them for discussion some definite programme for future organization.

It is clear that legislation already foreshadowed will set some fresh problems, but the nature of these cannot be exactly determined. In 1945 the position will be clearer for the Council to determine its future policy. It is in my mind that, additional to some minor changes in our routine of administration, it will be necessary to give full consideration to the problem of how tasks of research may be best co-ordinated in the new era which we are promised with the general provision of effective treatment of rheumatic sufferers.

Treatment

In the last Annual Report I chronicled the official pledge of the Government in post-war health policy "to ensure that all will receive the treatment appropriate to their needs." There were some doubters who thought that this might be interpreted, in the spirit of the Lord Chancellor in *Iolanthe*, to mean "all, except that very large section of the community which has the misfortune to suffer from rheumatic disease." Perhaps in their minds was a memory of the original National Health Insurance Act, which purported to provide for the medical needs of the under-privileged sections of the community. The Act implicitly recognized that research into the causation and the most efficient form of treatment of rheumatism called for special measures other than those available to the general practitioner or the general hospital, since provision was made, for the approval by the Minister of Health, of institutions equipped to provide those special measures. But the number of institutions approved was trifling; it never reached double figures. Further, an approved society under the Act could pay for rheumatism treatment only if its finances were so prosperous that it had a surplus after meeting all other calls; then rheumatism treatment could be provided as an "additional benefit." The effect was that only those who were insured with a prosperous society *and* were within reach of one of the very few approved clinics could benefit—a very small percentage of the total. But we are assured that there is no justification for such cynical doubts; that the Ministry really intends to deal effectively with the treatment of rheumatic disease—on the whole the most serious enemy of health and industrial efficiency in our community.

The Minister of Health has set up a sub-committee of his Medical Advisory Committee to consider the whole position relative to rheumatism treatment and to report to him for his guidance. On this sub-committee the Empire Rheumatism Council is fully represented.

Post-Graduate Education

Consequent on the decision to extend the benefit of treatment to all rheumatic sufferers, it is to be expected that in the post-war period there will be a demand exceeding the supply at present available of medical practitioners with some special knowledge of rheumatic diseases. The Empire Rheumatism Council (*vide* Annual Report, 1942) recognized its responsibility to help to meet this need. Your War Emergency Committee during the past year has taken preliminary steps to that end, and, with the

greatly appreciated help of medical bodies having a special interest in the problems of rheumatism, has organized a Committee on Post-Graduate Education, of which Sir Adolphe Abrahams has very kindly consented to act as Chairman.

It has been made clear that the Empire Rheumatism Council has no intention of attempting to trespass on the field of other institutions. The task of ensuring that the medical profession as a whole is trained to deal effectively with the problems of rheumatic disease must be ultimately the responsibility of the medical teaching schools. Our part is to stimulate; to keep up the pressure of public opinion for action, and, to the extent that is necessary, to help temporary measures to meet emergency needs.

Research

The discovery of the great efficacy of preparations of the mould penicillin in dealing with certain infective conditions naturally led to inquiries as to whether it would prove valuable in the treatment of some forms of rheumatic disease. A limited test undertaken by Surgeon-Commander C. A. Green, of our Naval Research Foundation, gave no encouragement. Further tests will be made when greater supplies of penicillin are available. His present results are confirmed by tests in the United States.

A claim was published during the year in a reputable American publication (which has a British-printed edition) that a preparation containing massive doses of vitamin D had proved to be a cure for rheumatoid arthritis. The claim was supported by citation of what seemed to be weighty medical authority. We had a spate of inquiries from individuals, newspapers, and institutions, which were answered cautiously as we were confident that our allied body, the American Rheumatism Association, would have communicated to us promptly any definite discovery. We were on the point of asking them for confirmation when the claim was officially condemned and publication of it censured by the American Medical Association. Inquiry early in October to one of the chief American drug manufacturers elicited that the preparation was no longer available in this country.

To several hundreds of correspondents who wrote during the year regarding the Russian serum mentioned in our last Annual Report we have had to send the disappointing reply that an investigation (limited by the very small supply made available) did not justify recommendation of its use. In view of the high reputation of Soviet medical research, we propose, so soon as war conditions permit, to invite the Russian scientist responsible for the serum to visit this country or, alternatively, for the Council to send a research worker to Moscow to make further investigations. Members will agree that, whilst it is our duty to test any suggestion which offers hope, it is also our duty to take the utmost care that mistaken or unproven claims are not given sanction.

We look forward to great progress in the field of clinical research when the establishment of a national chain of treatment centres will enable comprehensive tests under full control conditions to be made for evaluating present means and proposed new means of treatment. The work of our Travelling Scholars, before the outbreak of the war, in studying the systems of the chief treatment centres of Europe and the United States was a valuable beginning. It showed that there was no lack of knowledge of modern methods in the British medical profession, but that, abroad as well as here, there was lack of what I shall call a determinative system, combining the highest degree of efficiency with reasonable regard for economy and for national habit. To institute such a system there is need, additional to diligent laboratory research, for exhaustive clinical research covering thousands of cases, accurately diagnosed and carefully observed.

Propaganda

Our Official Journal, *The Annals of the Rheumatic Diseases*, will be published in future quarterly by the British Medical Association. We hope that this will lead to a wider interest in the *Annals* among the general body of the medical profession. The first number under the new arrangement was published in September. The Editorial Board remains as before, strengthened by the addition of the Editor of the *British Medical Journal*. There will be no departure from the close association in its publication with our colleagues of the American Rheumatism Association. I am confident that all members of the Council will wish to express their gratitude to the Editors of the Journal for their devoted work during the past five years. They have kept the flag flying during a time when it was extremely difficult for medical scientists to give close attention to the campaign against rheumatism. No other medical publication dealing specially with the problems of rheumatism has survived in Western Europe during the war.

Mention of the Journal leads me to express once more on behalf of the Council thanks to the medical and lay Press for the help they have continued to give to our work. This help, during a period when printing paper was more severely rationed than most other amenities of life, has remained consistently generous.

Opportunities for educational meetings have been scanty but all that were offered have been taken.

A Fourth Edition of " Rheumatism—A Plan for National Action " was published in October, previous editions, totalling 6,000 copies, having been exhausted.

Administration

Administrative work has been heavy during the year, our Council having been accepted by the public as a kind of unofficial mentor on rheumatism questions. Answering inquiries as to treatment care is taken to advise reference to the family doctor, and

to add what helpful information can be given. Frequent grateful letters from medical practitioners and from sufferers come as a reward. No trouble is spared in seeking out statistical and other information required, but a polite firmness is necessary when we are asked, for example, to study the measurements of the Pyramids in relation to rheumatic disease or to finance a research to prove that one certain type of apple will infallibly cure rheumatism. I am confident that all members will join me in expressing gratitude for the work of the War Emergency Committee—viz., Dr. C. W. Buckley, Dr. Hugh Burt, Lt.-Col. W. S. C. Copeman, A. G. Timbrell Fisher, Dr. Mervyn H. Gordon, Col. the Rt. Hon. Lord Gretton, Brig. F. D. Howitt, Sir Walter S. Kinnear, T. W. Robinson, and H. Gordon Thompson. Their responsibilities during the war years in acting for all the regular standing committees of the Council have been onerous. Next year should see the re-constitution of those Committees.

We shall soon now be emerging from the dust and din of battle after overcoming the grimmest threat to mankind's well-being that history records. As the dawn of victory shows on the horizon, plans multiply to provide, as a reward for the sacrifices of the past, some secure hope for future well-being. To abolish the tragedy of vast mutual slaughter among the race of Man is certainly the first necessity. Additional to that, those plans give the highest promise of significant value which, in the field of social medicine, enlist the energies of peoples to combat the forces of killing and crippling disease. " Waste not, want not " is the basic law of economic advance, and there is no more cruel waste than permitting the wide incidence of avoidable illness. In that field of social medicine lies our task. The progress, achieved in the past difficult years gives me confidence that, if we maintain our energy, we may, within a reasonable term, see the happy end of our labours.

HORDER,
Chairman,

FRANK FOX,
Secretary.

THE PAN-AMERICAN LEAGUE FOR THE STUDY AND CONTROL OF RHEUMATIC DISEASES

BY

LORING T. SWAIM

There has recently been established a Pan-American League for the Study and Control of Rheumatic Diseases, consisting of the following countries: Argentina, Brazil, Canada, Chile, Mexico, Paraguay, Peru, Uruguay, United States of America. The officers of the League are: *President*.—Dr. Ralph Pemberton, Philadelphia, Pa., U.S.A.; *Vice-President*.—Dr. Anibal Ruiz-Moreno, Buenos Aires, Argentine, S.A.; *Secretary*—Dr. Loring T. Swaim, Boston, Mass., U.S.A.; *Treasurer*—Dr. Fernando Herrera Ramos, Montevideo, Uruguay, S.A. The full list of delegates to the Central Committee of the League from the various countries is not yet at hand. However, so far as the United States is concerned, the following have been appointed: Lt.-Col. Philip S. Hench (M.C., U.S. Army); Dr. Richard H. Freyberg. Representatives to the Regional Committee are: Col. Walter Bauer (M.C., U.S. Army); Dr. Donald F. Hill.

The objectives of the Pan-American League as drawn up in the Statutes are as follows: "(*a*) to strengthen the cultural bonds between the countries of North and South America; (*b*) to further efforts to alleviate suffering from rheumatic diseases and to institute measures of prevention; (*c*) to compile and disseminate knowledge and information regarding rheumatism in the respective countries; (*d*) to unify the nomenclature and classifications; (*e*) to promote scientific investigation; (*f*) to hold Pan-American Congresses on the rheumatic diseases".

It is obvious, of course, that at the present time —and perhaps for some time to come—the holding of a congress will be out of the question because of difficulties of transportation. In spite of this, it is clear from experience acquired during development of the League that much can be, and indeed has already been, accomplished, chiefly by correspondence, in the direction of implementing the League's purposes, at least in a preliminary way. In some countries comprising the League distinct impetus has been given to consideration by the medical profession of the large group of conditions coming under the head of rheumatic diseases. In certain other countries interest has been created where apparently little or none existed before, so that from the broad sociologic standpoint definite gains have been recorded which might otherwise have required many years for development.

Another result forthcoming from the international correspondence necessarily involved in forming the League is inauguration of a correlation of clinical experiences in several of the countries concerned, bearing upon the types of rheumatism encountered and the races in which they occur. Hardly a beginning has been made in this connection, but the way is now open for exploration of the incidence of rheumatic diseases under the varied conditions of climate, altitude, race, and nutrition, which are involved in the wide area covered by the League's interests, extending as they do from Hudson Bay to Tierra del Fuego. An extensive and critical study of such a condition as rheumatic fever in subtropical and tropical countries would doubtless reveal facts of great significance. Perhaps nothing of greater importance presents before the League than that of obtaining full and accurate statistics bearing upon the several problems just mentioned. It is hoped that those physicians privileged to take part in the forward looking movement constituting the Pan-American League will turn their energies at an early moment to this end. A way must of course be found for making available to all the members of the League such statistics and correlations of clinical experiences as may develop, though at the moment the means to this end are not clearly indicated. Several possibilities are under consideration, however, and it is expected that in course of time this desideratum will become an actuality. Many other examples could be cited of the advantages already gained by contact, even by mail, between the various workers in this field in the several countries concerned.

With establishment of the Pan-American League, which had its incipiency with Dr. Anibal Ruiz-Moreno and his colleagues in Buenos Aires, something should be said as to its relation to the Ligue Internationale contre le Rhumatisme from which, indirectly, it sprang. The original prospectus of the Pan-American League expressly set forth that it is in no sense meant to act as a substitute for the Ligue Internationale but rather as an amplification and implementation of the older Ligue's purposes. It is abundantly clear that for the present, and presumably for some time to come, many of the nations of Europe will not be able to further effectively the objectives and activities of the Ligue Internationale. In a sense, therefore, the Pan-American League can

be regarded as the child of the Ligue Internationale, having among its other functions that of keeping alive and developing international interest and collaboration in the field of rheumatic disease. When peace finally reigns throughout the world the Pan-American League can then take its place as an integral though discrete part of the older organization. On the other side of the picture it is clear that the war has provided intensive and additional experience in the armies of some of the countries involved, as to the incidence and nature of certain phases of the major problem—for example, rheumatic fever, so-called psychogenic rheumatism, psycho-somatic rheumatism, and fibrositis and it would be highly desirable as soon as practicable to extend to all countries of the Pan-American League as full information, in these connections, as may be available for prevention and control.

One other point needs comment—namely, in regard to paragraphs (*a*) and (*c*) of the objectives of the Pan-American League. The influence of co-operation in the world of science is by definition limited in a political sense, but co-operation nevertheless may contribute to a rapprochement which often transcends all barriers. It is not too much to hope, therefore, that the Pan-American League will exercise at least a tacit influence in the direction of international amity.

Finally, in spite of the limitations imposed upon travel, it is hoped that members of those countries in which rheumatic diseases have not been intensively studied will feel inclined to visit those other countries where, of necessity, these diseases have compelled and obtained active attention from both the lay and medical public. So far as the United States is concerned, the officers and members of the American Rheumatism Association would welcome visits from any of their colleagues in the other Americas and would deem it a privilege to show them whatever may be going on of interest.